ATTACHMENT A
Remarks

Claims 1-16 are pending in the present application and claims 17-43 are withdrawn from consideration. By this Amendment, Applicants have amended claims 1, 6 and 11-14. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

The specification was objected to for including informalities. For example, claim 1 was objected to for including the acronym Ulip/CRMP and the disclosure was objected for using the abbreviation "SEQ ID n°" rather than "SEQ ID NO:". By this Amendment, Applicants have amended claim 1 by including the full names for Ulip and CRMP and amended the specification by replacing "SEQ ID n°" with SEQ ID NO:" thereby obviating these rejections.

The Examiner noted typographical errors on page 7 and page 28. However, upon carefully reviewing these pages, Applicants find no errors.

Finally, with regard to the specification objections, the Examiner alleges that the application does not include an Abstract of the Disclosure. However, contrary to the Examiner's assertion, the present application did include an Abstract of the Disclosure on page 82. However, in order for the Abstract of the Disclosure to be more consistent with 37 C.F.R. § 1.72, Applicants have submitted a Substitute Abstract along with this Amendment to the specification.

Claim 6 was objected to for being in improper Markush group from alleging that the claim includes a Markush group having the conjunction "and" twice. Contrary to the Examiner's assertion, the second "and" of claim 6 (original) was not part of the Markush

group but part of the method claim itself. In order to more clearly recite the Markush group, Applicants have amended claim 6 by replacing the second "and" with the phrase "along with" thereby providing further clarity to claim 6 and obviating the objection.

Claims 6-16 were rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. The Examiner alleges that claim 6, drawn to a method of "administering to a patient...a therapeutically effective amount" is directed to the use of a therapeutic compound of which the specification does not contain examples of administering that compound *in vivo* to prevent or treat the claimed myelin disorders. The Examiner admits that the specification includes an example of an *in vitro* example of administering antibodies to CRMP2 and CRMP5 which resulted in the reduction of Sema3A inhibition of axonal process extension. However, the Examiner alleges that the specification via this single example does not provide a complete disclosure of a representative number of possible therapeutic agents which the claims encompass, to convince one skilled in the art that the Applicants are in possession of the claimed treatment.

Contrary to the Examiner's allegation, the present invention as recited in claims 6-16 is directed to a method for the prevention or treatment of myelin disorders by administering a therapeutic compound which is described in the specification so as to establish the Applicants were in possession of the claimed invention. Disclosed in the present application, the present inventors have identified Ulip/CRMP (hereinafter "CRMP") as a new target for preventing or treating a myelin disorder. For example, the inventors have shown that the CRMP protein family, e.g., CRMP5 and/or CRMP2 is/are involved in myelination, demyelination, remyelination in the central nervous system

(see, e.g., page 2, lines 15-18). In human adults, members of the CRMP family have been implicated in human neurogenerative diseases and disorders. (Specification, page 1, lines 30-31.)

The specification further describes examples of the claimed modulating agents which control the expression of myelin. For example, the present specification discloses various screening methods for identifying modulating agents. One screening process includes identifying agents useful for the prevention or treatment of myelin disorders by contacting a CRMP protein with a test compound, determining the test compound has a modulatory effect on the CRMP activity and identifying those compounds having a stimulatory or inhibitory effect on the CRMP protein as useful for the prevention or treatment of myelin disorder. See, e.g., page 17, line 5 to page 18, line 13. Accordingly, the aforementioned screening process fully describes modulating agents which would be effective for use in the claimed treatment of myelin disorders. Thus, the specification provides a sufficient written description for one of ordinary skill in the art to know what modulating agents could be used in the claimed method, in accordance with the written description requirement articulated in *University of Rochester v. G.D. Searke & Co., Inc.,* 69 U.S.P.Q.2d 1886 (Fed. Cir. 2004).

Moreover, one of ordinary skill in the art upon reading the present specification would recognize that modulating agents, e.g., the specifically claimed proteins, nucleic acids and antibodies, could be useful for controlling the expression of myelin, and, by controlling the expression of myelin, one can treat myelin disorders. Based on what was known in the prior art before the present invention with regard to CRMP's presence in neuron cells and the present discovery that the CRMP protein family is involved with

myelination, demyelination and remyelination in the central nervous system, one of ordinary skill in the art would recognize the Applicants had possession of the invention, namely treatment of myelin disorders via administering a CRMP modulating agent, as claimed. Therefore, Applicants respectfully request that the rejection to claims 6-16 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 1-16 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner alleges that the subject matter is not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains to make and/or use the invention.

Although the Examiner alleges that undue experimentation would be necessary in order for one of ordinary skill in the art to practice the claimed invention, the present invention is fully enabled by the specification so that one of ordinary skill in the art and familiar with this field can practice the invention as claimed. Support for enablement of the present invention is provided by the attached two Declarations Under Rule 132.[1] One Declaration from the inventor Dr. Marie-Françoise Belin, (hereinafter "Belin Declaration") demonstrates that the onset of EAE (model of multiple sclerosis) in CRMP1-deficient mice is delayed in comparison to control mice, thereby highlighting the key role of CRMPs in the myelination/demyelination processes. The second Declaration is from an expert in the field, Dr. Zalc, (hereinafter "Zalc Declaration") who explains why the results set forth by the inventors provide a rationale of the new therapeutic pathway, thereby supporting applicant's contention that one skilled in the art would both be enabled to practice the invention in accordance with §112, ¶1

[1] Executed copies of these Declarations will be filed shortly.

(enablement), and reorganize the inventors were in possession of the invention at the time of filing the patent application in accordance with §112, ¶1 (written description). Executed copies of the two Declarations will be filed with the U.S. Patent Office in due course once received.

With regard to the Belin Declaration, Dr. Belin establishes that using CRMP1 deficient mice with injected MOG (a classic animal model for MS), the CRMP1-deficient mice showed the first clinical symptoms of EAE (experimental allergic encephalomyelitis), more than 12 days later than in the control mice. The modulation of CRMP during demyelination in this an experimental model of MS indicates the involvement of CRMP in demyelination. In addition, the test results show that CRMP2 expression is unregulated while CRMP5 is down-regulated in animals with EAE compared to healthy untreated animals. Thus, the Belin Declaration establishes a link between CRMP modulation and myelin disorders. See Belin Declaration, page 3.

The Zalc Declaration further establishes that one of ordinary skill in the art would be able to practice the invention as claimed. In particular, the Zalc Declaration demonstrates that modulating CRMP activity is relevant for the prevention and treatment of myelin disorders. The Zalc Declaration first notes that the inventors found that CRMPs are key players in the transduction of signals acting on oligodendrocytes, the myelin forming cells in the central nervous system. Further, the Zalc Declaration demonstrates that the data disclosed in the specification demonstrates the involvement of CRMP-mediated signalization at the time of myelin formation. Further, the Zalc Declaration notes that CRMP appears at the crossroads of several different signalization pathways, which are activated at the time of the myelin deposition, i.e., at

the time during development of oligodendrocyte processes wraps around the axon to generate the myelin sheath.

The Zalc Declaration concludes, based on the specification and what was known in the art, CRMPs are a new target for increasing myelin formation and thus remyelination. The Zalc Declaration further notes that since myelin acts as an insulator of axons and demyelination results in nerve cell conduction blockage, remyelination is critical to reestablishing normal nerve conditions. Thus, using the modulation of CRMPs disclosed in the specification and claimed does provide an enabled new therapeutic pathway for the prevention and treatment of myelin disorders. See, Zalc Declaration, page 2, third paragraph to page 3, first full paragraph.

Based on the foregoing, Applicants respectfully submit that the present invention as recited in claims 1-16 are fully enabled in accordance with 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request that the rejection to these claims be withdrawn.

Based on the foregoing, Applicants respectfully submit that the present application is in condition for allowance.

END REMARKS